

REMARKS

The Office Action dated July 30, 2003 has been received and carefully noted. The above amendments and the following remarks are submitted as a full and complete response thereto.

Claims 1-3, 5, 7, 8, 15, and 17-25 are pending. Claims 1-3, 5, 7, 8, 15, and 17-25 are rejected. Claims 4, 6, 9-14, and 16 were previously cancelled.

Applicant respectfully acknowledges that the Office has withdrawn the rejection under 35 U.S.C. §112, first paragraph, for scope of enablement, as it pertains to claims 1-3, 5, 7-8, 15, and 18-22. These actions are greatly appreciated.

Claim 23 remains rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter, which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. Claim 23 is also rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant respectfully addresses the two § 112 rejections jointly because these rejections essentially cover the same issues. The Office acknowledges that the Applicant has shown activity of the sublancin peptide against a wide variety of gram-positive bacteria, and has sufficiently provided a description for the generic claims. However, the Office argues that Applicant has not sufficiently disclosed a method of decontaminating a *Bacillus anthracis* (also known herein as "anthrax") spore containing

area as claimed in claim 23. The Office suggests that evidence of successful decontamination of these specific spores may overcome this rejection.

In the Response of March 26, 2003, Applicant argued that the Internet article (http://nano.med.umich.edu/Anti_infectives.html) states that *Bacillus cereus* can be used as a substitute for anthrax, and therefore the specification is enabling. Applicant argued that *B. cereus* is commonly used as a model system for the study of *Bacillus anthraxis* since *B. cereus* is a nearly harmless bacterium, unlike anthrax, and *B. cereus* is closely related to anthrax.

The Office takes the position that this argument is unpersuasive. The Office argues that use of the *B. cereus* model system is not a substitute for anthrax because it does not necessarily indicate that a compound of the present invention can be successfully used on anthrax. Applicant respectfully disagrees.

Applicant notes that the Internet reference states that *B. cereus* is commonly used as a model system for the study of anthrax. The Office has incorrectly characterized the disclosure of the Internet reference, and consequently, has mischaracterized the scope of the use of *B. cereus* as a substitute for anthrax as being limited to initial drug screening only. In contrast to the characterization of this reference by the Office, Applicant notes that the Internet reference discloses the following: 1) the study, which was the subject of the internet article, was itself an initial study; 2) the researchers of that study did not use anthrax because of the inherent danger of anthrax; 3) the researchers chose to use *B. cereus*, because it is a commonly known substitute (i.e., model system) for studying anthrax. Thus, the reference indicates that *B. cereus* was chosen not simply because the study was an initial study, but rather because the

bacterium is a known test substitute for *B. anthraxis*. The fact that *B. cereus* was used for the particular initial study of the reference does not limit *B. cereus* to initial studies in general. The reference does not support such a proposition. Applicant respectfully submits that the rejection is improper and requests that the rejection be withdrawn.

Claims 1-8 and 15-22 remain rejected under 35 U.S.C. §103(a) as being unpatentable over Paik in view of U.S. Patent No. 6,143,498 to Olsen et al ("Olsen"). The Office argues that Paik teaches the production of antimicrobial peptide sublancin-168 and the activity of the peptide against a variety of Gram positive or negative bacteria. In this obviousness rejection, the Office notes that Olsen is silent with regards to sublancin, and relies on Olsen to teach the addition of a histidine tag, also referred to herein as "His-tag," to an antimicrobial peptide in order to facilitate purification, a feature not disclosed in Paik. The Office contends that one of ordinary skill in the art at the time of the invention would have expected to utilize the same system as Olsen in order to obtain other His-tag antimicrobial peptides, such as the sublancin-168 of Paik.

The Office specifically argues that Olsen discloses in Example 1 that a certain commercially available expression vector contains six codons for histidine and that elements of the vector are arranged such that the histidine residues are attached to the carboxy end of an expressed polypeptide. In this construct, several codons are placed between the histidine codons and the carboxyl end of the peptide, meaning the expressed His-tag polypeptide contains a spacer between the carboxyl end of the peptide and the His-codons.

Applicant respectfully traverses the obviousness rejection. It is the position of Applicant that the combination of Paik and Olsen does not render obvious the present

invention. As evidence, Applicant notes that the prior art discloses a low likelihood of success of His-tagging lantibiotics. Applicant has already expanded upon this argument in the specification (page 6, paragraph 30) and the Response of March 26, 2003 on pages 6-7 (referring especially to the Rodriguez thesis).

In addition and in contrast to the prior art, Applicant points to the unexpected results achieved by the present invention. Applicant has successfully labeled the C-terminus of the lantibiotic sublancin with the histidine tag and the activity of the lantibiotic is retained.

Applicant respectfully notes that the obviousness rejection appears to ignore the supplemental response of May 9, 2003, which presents relevant portions of the Rodriguez thesis. Applicant notes that the data presented in the Rodriguez thesis is pertinent to the obviousness rejection, and therefore, requests that the Office consider the Rodriguez thesis.

The Rodriguez thesis supports the contention that Applicant achieved unexpected results in labeling the sublancin polypeptide with a histidine tag. The thesis outlines the methods and result of attempting to produce a histidine-tagged subtilin peptide. The thesis explicitly expresses the difficulty of producing the histidine-tagged subtilin peptide. See Rodriguez thesis, page 154, paragraph 1 to page 160, paragraph 2. In light of the Rodriguez thesis, the results achieved by the applicant are truly unexpected. Applicant's histidine tagging of sublancin-168 was not obvious, and therefore the rejection of the Office is without merit.

It is respectfully submitted that the finality of the action is improper in view of the fact that the supplemental response was not considered. Withdrawal of finality is respectfully requested.

The Office contends that the submission of a terminal disclaimer in this application contradicts Applicant's claim of unexpected results. The Office contends that the instant claims are obvious in light of sublaicin itself. The Office therefore states that the present invention cannot be both unexpected and obvious over the peptide itself.

Applicant respectfully disagrees. The filing of a Terminal Disclaimer does not act as an admission or acquiescence to the underlying double patenting rejection. The filing of a Terminal Disclaimer serves the statutory function of removing the rejection of double patenting, and raises neither presumption nor estoppel on the merits of the rejection. See *Ortho Pharm. Corp. v. Smith*, 959 F.2d 936, 941-42 (Fed Cir 1992); *Quad Envtl. Tech. Corp. v. Union Sanitary Dist.*, 946 F.2d 870, 874 (Fed Cir 1991). It is improper to convert this simple expedient of "obviation" into an admission of acquiescence or estoppel on the merits. See *id.* A terminal disclaimer is of circumscribed availability and effect, and it is not an admission of obviousness of a later-filed claimed invention in light of an earlier-filed disclosure. See *Quad*, 946 F.2d at 874.


In view of the foregoing, reconsideration of the application, withdrawal of the outstanding rejections, allowance of claims 1-3, 5, 7, 8, 15, and 17-25, and the prompt issuance of a Notice of Allowability are respectfully solicited.

If this application is not in condition for allowance, the Office is requested to contact the undersigned at the telephone listed below.

In the event this paper is not considered to be timely filed, the Applicant(s) respectfully petition(s) for an appropriate extension of time. Any fees for such an extension, together with any additional fees that may be due with respect to this paper, may be charged to counsel's Deposit Account No. 01-2300, **referencing docket number 108172-00058.**

Respectfully submitted,

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